Rejection of Claims 13, 19, 32, and 38 Under 35 U.S.C. § 112, First Paragraph

Claims 13, 19, 32, and 38 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly based on a disclosure that is not enabling because of improper incorporation of essential subject matter by reference. Specifically, the Examiner states that the attempt to incorporate essential subject matter into this application by reference to a list of genes with only some GenBank Accession Numbers is improper because the reference is neither a U.S. Patent application or a U.S. Patent. The rejection is respectfully traversed.

Claims 13, 19, 32, and 38, as amended herein, recite methods of identifying intestinal polyps by determining the expression profile of at least three informative nucleic acid molecules, wherein the informative nucleic acid molecules are selected from the nucleic acid molecules in Figures 1A-1U. Figures 1A-1U are a table listing the nucleic acid molecules that are differentially expressed in intestinal polyps and normal intestinal tissues. The name of each nucleic acid molecule is provided in Figures 1A-1U. In addition, the Accession (GenBank or Affymetrix) number is also provided for each nucleic acid molecule.

While Claims 13, 19, 32 and 38 are rejected based on an alleged improper incorporation of essential subject matter by reference, Applicants submit that no attempt to incorporate subject matter has been made, in that Applicants have not attempted to incorporate the sequences of the referenced nucleic acid molecules into the application. Rather, the names of the nucleic acid molecules indicate to one of skill in the art the nature of the nucleic acid molecules, much as the nature of a chemical compound is known to one of skill in the art merely by reference to its name. That is, one of skill in the art could readily obtain additional information regarding the specified nucleic acid molecule, *e.g.*, the nucleotide sequence, if desired, by reference to a number of sources, including the GenBank database, the Affymetrix database, the TIGR database, and myriad published papers and other databases, in the same way that one of skill in the chemical arts could obtain additional information about a chemical compound by referring to, for example, the IUPAC nomenclature of organic compounds. The GenBank and Affymetrix Accession numbers are provided in Figures 1A-1U merely as an additional aid to the skilled artisan. Based on this knowledge in the art and the added information provided in the Specification, one of skill in the art can readily practice the invention as claimed. Accordingly,

Applicants respectfully submit that the rejection is unfounded, and reconsideration and withdrawal of the rejection are respectfully requested.

Double Patenting Rejections

Claims 1-3, 14-16, 20-22, and 33-35 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 111 of U.S. Patent Application No. 09/544,627. The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the broad claim of diagnosing any disease of any individual by comparing any kind of change in the gene expression as compared to a control as claimed in Claim 111 of U.S. Application No. 09/544,627 encompasses the instant claims of identifying an intestinal or colonic polyp by determining increased or decreased expression of the gene. This rejection is traversed as follows.

Applicants first note that U.S. Patent Application No. 09/544,627 is a pending application. Applicants believe that if a rejection is made by the Examiner, the rejection should be a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. As stated in the M.P.E.P. (804, I, B):

> Occasionally, the examiner becomes aware of two copending applications filed by the same inventive entity, or by different inventive entities having a common inventor, and/or by a common assignee that would raise an issue of double-patenting if one of the applications became a patent. Where this issue can be addressed without violating the confidential status of applications (35 U.S.C. 122), the courts have sanctioned the practice of making applicant aware of the potential double patenting problem if one of the applications became a patent by permitting the examiner to make a "provisional" rejection on the ground of double patenting.

> The M.P.E.P. (804, I, B) further states:
> The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications. If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional"

double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

Based on the belief that the above double patenting rejection is a provisional rejection, this provisional rejection will be addressed as necessary upon an indication of allowable subject matter in this application and/or U.S. Patent Application No. 09/544,627.

Applicants note, however, that Claim 111 of U.S. Patent Application No. 09/544,627 was canceled in an Amendment A, filed in that application on May 23, 2002 (copies of U.S. Patent Application No. 09/544,627 and the claims as currently pending are submitted herewith in a Supplemental Information Disclosure Statement). As stated in the M.P.E.P. (804 II, B, 1), "Obviousness-type double patenting requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent." (emphasis added). Because Claim 111 of U.S. Patent Application No. 09/544,627 has been cancelled, Applicants believe that this provisional double patenting rejection has been obviated.

Claims 4-7, 10-12, 17-18, 23-26, 29-31, and 36-37 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 111 of U.S. Patent Application No. 09/544,627 in view of Holmes (U.S. Patent No. 5,403,717). As discussed above, since the primary conflicting reference is an application, Applicants submit that this rejection is a *provisional* double patenting rejection. As such, this rejection will be addressed as necessary upon an indication of allowable subject matter in this application and/or U.S. Patent Application No. 09/544,627. Furthermore, Applicants again note that Claim 111 of U.S. Patent Application No. 09/544,627 has been cancelled, thus obviating the provisional rejection.

Claims 8, 9, 27, and 28 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 111 of U.S. Patent Application No. 09/544,627 in view of Holmes (U.S. Patent No. 5,403,717), and further in view of Arnold *et al.* (U.S. Patent No. 6,423,535 B1). Again, since the primary conflicting reference is an application, Applicants submit that this rejection is a *provisional* double

patenting rejection. Thus, this rejection will be addressed as necessary upon an indication of allowable subject matter in this application and/or U.S. Patent Application No. 09/544,627. In addition, Applicants again note that Claim 111 of U.S. Patent Application No. 09/544,627 has been cancelled, thus obviating the provisional rejection.

Claims 13, 19, 32, and 38 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 111 of U.S. Patent Application No. 09/544,627 in view of Holmes (U.S. Patent No. 5,403,717), and further in view of Lee *et al.* (Hepatology 19(3):656-665, 1994). Again, since the primary conflicting reference is an application, Applicants submit that this rejection is a *provisional* double patenting rejection. Accordingly, this rejection will be addressed as necessary upon an indication of allowable subject matter in this application and/or U.S. Patent Application No. 09/544,627. In addition, Applicants again note that Claim 111 of U.S. Patent Application No. 09/544,627 has been cancelled, thus obviating the provisional rejection.

Rejection of Claims 1, 4-7, 10-12, 14, and 17-18 Under 35 U.S.C. § 102(e)

Claims 1, 4-7, 10-12, 14, and 17-18 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Reinhard *et al.* (U.S. Patent No. 6,432,668 B1; hereafter "Reinhard"). The Examiner states that Reinhard teaches a method of identifying an intestinal polyp comprising the steps of a) obtaining a nucleic acid sample derived from intestinal tissue; and b) determining a gene expression profile from a gene expression product of at least one informative gene having increased expression in an intestinal polyp relative to a control, the gene expression product being a DNA, mRNA, or polypeptide, wherein increased expression of the gene in the sample is indicative of an intestinal polyp. The rejection is addressed as follows.

Reinhard discloses a human gene encoding a cyclin-dependent kinase named hPFTAIRE. Reinhard also discloses methods of diagnosing or prognosticating neoplasia in a mammal by measuring hPFTAIRE gene or protein expression in a first tissue suspected of being neoplastic and comparing it with hPFTAIRE gene or protein expression in a second normal tissue. Over-expression of the hPFTAIRE gene in the first tissue compared to the second tissue indicates neoplasia in the first tissue.

Claim 1 has been amended herein to recite a method of identifying an intestinal polyp comprising the steps of: a) obtaining a nucleic acid sample derived from intestinal tissue; and b) determining an expression profile from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control, wherein increased expression of the nucleic acid molecules in the sample is indicative of an intestinal polyp. In addition, Claim 14 has been amended herein to recite a method of identifying an intestinal polyp comprising the steps of: a) obtaining a polypeptide sample derived from intestinal tissue; and b) determining an expression profile from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control, the expression products being polypeptides, wherein increased expression of the expression products in the sample is indicative of an intestinal polyp.

As Reinhard discloses neoplasia diagnostic and prognostic methods by assessing the expression of only one nucleic acid molecule or one nucleic acid molecule product, Reinhard does not anticipate Claim 1 or Claim 14 as amended herein. Furthermore, Claims 4-7 and 10-12 depend from Claim 1, and Claims 17-18 depend from Claim 14, and are therefore subject to the limitations of Claims 1 and 14, respectively. Thus, Reinhold does not anticipate any of Claims 4-7, 10-12, and 17-18. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-7, 10-12, and 14-18 Under 35 U.S.C. § 102(b)

Claims 1-7, 10-12, and 14-18 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Holmes *et al.* (U.S. Patent No. 5,403,717; hereafter "Holmes"). The Examiner states that Holmes teaches a method of identifying an intestinal polyp comprising the steps of a) obtaining a nucleic acid sample derived from intestinal tissue; and b) determining a gene expression profile from a gene expression product of at least one informative gene having increased expression in an intestinal polyp relative to a control, the gene expression product being a DNA, mRNA, or polypeptide, wherein increased expression of the gene in the sample is indicative of an intestinal polyp. The rejection is addressed as follows.

Holmes discloses diagnostic and prognostic methods for monitoring premalignant or malignant conditions of human secretory epithelia, for example, colonic epithelia, by determining the extent of expression of β1-3N-acetylglucosaminyltransferase.

Claim 1 has been amended herein to recite a method of identifying an intestinal polyp comprising the steps of: a) obtaining a nucleic acid sample derived from intestinal tissue; and b) determining an expression profile from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control, wherein increased expression of the nucleic acid molecules in the sample is indicative of an intestinal polyp. Furthermore, Claim 14 has been amended herein to recite a method of identifying an intestinal polyp comprising the steps of: a) obtaining a polypeptide sample derived from intestinal tissue; and b) determining an expression profile from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control, the expression products being polypeptides, wherein increased expression of the expression products in the sample is indicative of an intestinal polyp.

As Holmes discloses methods of diagnosing or prognosticating by assessing the expression of only one nucleic acid molecule or one nucleic acid molecule product, Holmes does not anticipate Claim 1 or Claim 14 as amended herein. In addition, Claims 2-7 and 10-12 depend from Claim 1, and Claims 15-18 depend from Claim 14, and are therefore subject to the limitations of Claims 1 and 14, respectively. Therefore, Holmes does not anticipate any of Claims 2-7, 10-12, and 15-18. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 8 and 9 Under 35 U.S.C. § 103(a)

Claims 8 and 9 stand rejected under 35 U.S.C. § 103(a) over Reinhard, or in the alternative Holmes, in view of Arnold *et al.* (U.S. Patent No. 6,423,535 B1; "hereafter "Arnold"). The Examiner states that Reinhard, or in the alternative Holmes, teaches the invention as recited in Claims 1 and 4-7, but they do not teach the method of Claim 1, wherein the gene expression profile is determined utilizing oligonucleotide microarrays, as recited in Claims 8 and 9. The Examiner further states that Arnold teaches a method of

determining a gene expression profile using oligonucleotide microarrays, and that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine and substitute a method wherein the gene expression profile is determined utilizing the oligonucleotide microarrays of Arnold in the method of Reinhard or Holmes. The rejection is addressed as follows.

Claim 1 has been amended herein to recite a method of identifying an intestinal polyp wherein an expression profile is determined from expression products of at least three informative nucleic acid molecules. As stated in M.P.E.P. 2143, to establish a *prima facie* case of obviousness, three basic criteria are required: 1) there must be some suggestion or motivation in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. Furthermore, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicants' disclosure. For the reasons set forth below, the combined references of Reinhard, or in the alternative Holmes, and Arnold do not meet these criteria, and thus do not render the claimed invention obvious.

The teachings of Reinhard and Holmes are as described above. Arnold discloses methods for normalizing and quantitating hybridization reactions by contacting distinct polynucleotide targets and standard polynucleotide targets with detectable nucleic acid probes complementary to the distinct targets and independently, detectable complements to the standard targets, to produce a hybridization pattern. The hybridization pattern is then detected and used to obtain information, including quantitative information, about the amount of polynucleotides in the sample. Arnold also discloses that the distinct and standard polynucleotide target can be attached to an array or a microarray and that the sample can be deposited on the array or microarray and hybridized to the probes. Arnold does not teach or suggest that the methods can be used to identify an intestinal polyp as recited in Claim 1.

The Combined References of Reinhard, Holmes, and Arnold Do Not Teach All of the Limitations of Claims 8 and 9

Claims 8 and 9 depend from Claim 1, which has been amended herein to recite a method of identifying an intestinal polyp comprising the steps of: a) obtaining a nucleic acid sample derived from intestinal tissue; and b) determining an expression profile from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control, wherein increased expression of the nucleic acid molecules in the sample is indicative of an intestinal polyp. Applicants assert that the combined references of Reinhard, Holmes, and Arnold do not teach all of the limitations of Claim 1, and therefore do not teach all of the limitations of Claims 8 and 9. As discussed above, Claim 1, as amended herein, requires that an expression profile be determined from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp, and neither Reinhard nor Holmes teach this claim element.

Arnold does not compensate for the deficiencies of Reinhard and Holmes. Arnold does not teach any methods for identifying an intestinal polyp, let alone how many informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control should be evaluated in order to determine an expression profile. Thus, Applicants submit that the combined references of Reinhard, Holmes, and Arnold do not teach every limitation of Claim 1. As Claims 8 and 9 depend from Claim 1, Applicants further assert that the combined references do not render Claims 8 and 9 obvious. On this basis alone, the rejection of Claims 8 and 9 should be withdrawn.

The Combined References of Reinhard, Holmes, and Arnold Do Not Provide a Suggestion or Motivation to Modify the References or Combine the Reference Teachings

Applicants submit that the combined references of Reinhard, Holmes, and Arnold do not provide a suggestion or motivation to modify or combine the teachings of the references to obtain the invention as recited in Claims 8 and 9. Neither Reinhard or Holmes suggests that expression levels of expression products other than the one gene disclosed in each respective reference should be evaluated in order to identify intestinal polyps. Arnold does

not make up for this deficiency; Arnold does not teach or suggest that an intestinal polyp can be identified using the described polynucleotide quantitation methods, nor does Arnold disclose three, two, or even one nucleic acid molecule that has increased expression in an intestinal polyp compared to a control. Thus, neither Reinhard, Holmes, nor Arnold provide a suggestion or motivation to combine or modify any of the references to obtain the invention as recited in Claims 8 or 9.

Rejection of Claims 13 and 19 Under 35 U.S.C. § 103(a)

Claims 13 and 19 stand rejected under 35 U.S.C. § 103(a) over Reinhard, or in the alternative Holmes, in view of Lee *et al.* (Hepatology 19(3):656-665, 1994; "hereafter "Lee"). The Examiner states that Reinhard, or in the alternative Holmes, teaches the invention as recited in Claims 1 and 4-7, but they do not teach the method of Claim 1, wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1U, as recited in Claims 13 and 19. The Examiner further states that Lee teaches "a method wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1U (GenBank Accession Number X67493; abstract, materials and Methods and Figures 1-2)," and that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine and substitute the method wherein one or more informative genes is selected from the group consisting of the genes in Figures 1A-1U in the method of Reinhard or Holmes. The rejection is addressed as follows.

As noted above, Claim 1 (from which Claim 13 depends) has been amended herein to recite a method of identifying an intestinal polyp wherein an expression profile is determined from expression products of at least three informative nucleic acid molecules. In addition, Claim 14 (from which Claim 19 depends) has been amended herein to recite a method of identifying an intestinal polyp wherein an expression profile is determined from expression products of at least three informative nucleic acid molecules, and wherein the expression products are polypeptides. Applicants submit that the three basic criteria for establishing a *prima facie* case of obviousness as described above have not been met by the combined references of Reinhard, or in the alternative Holmes, and Lee and thus, the references do not render the claimed invention obvious.

The teachings of Reinhard and Holmes are as described above. Lee discloses the cloning and sequence analysis of the murine insulin-like growth factor binding protein-1 (IGFBP-1) gene. In addition, Lee discloses that IGFBP-1 mRNA and protein levels are increased in liver tissue and serum during liver regeneration. Lee does not appear to teach that IGFBP-1 is expressed in intestinal tissue, nor does Lee teach or suggest that IGFBP-1 can be used to identify an intestinal polyp as recited in Claim 13.

The Combined References of Reinhard, Holmes, and Lee Do Not Teach All of the Limitations of Claims 13 and 19

Claim 13 depends from Claim 1, which has been amended herein to recite a method of identifying an intestinal polyp comprising the steps of: a) obtaining a nucleic acid sample derived from intestinal tissue; and b) determining an expression profile from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control, wherein increased expression of the nucleic acid molecules in the sample is indicative of an intestinal polyp. Claim 19 depends from Claim 14, which has been amended herein to recite a method of identifying an intestinal polyp comprising the steps of: a) obtaining a polypeptide sample derived from intestinal tissue; and b) determining an expression profile from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control, the expression products being polypeptides, wherein increased expression of the expression products in the sample is indicative of an intestinal polyp. Applicants assert that the combined references of Reinhard, Holmes, and Lee do not teach all of the limitations of Claims 1 or 14, and therefore do not teach all of the limitations of Claims 13 or 19. Claims 1 and 14, as amended herein, require that an expression profile be determined from expression products of at least three informative nucleic acid molecules having increased expression in an intestinal polyp, and neither Reinhard nor Holmes teach this claim element.

Lee does not make up for the deficiencies of Reinhard and Holmes. While the IGFBP-1 gene cloned by Lee is listed as an informative nucleic acid molecule in Figures 1A-1U of the present application, the data provided in Figures 1A-1U indicate that IGFBP is present in normal intestinal tissue and absent in intestinal polyps. Thus IGFBP-1 is not an

informative nucleic acid molecule having increased expression in an intestinal polyp relative to a control as required by each of Claims 13 and 19. Thus, Applicants submit that the combined references of Reinhard, Holmes, and Lee do not teach every limitation of Claims 13 and 19, which require determining the expression level of at least three informative nucleic acid molecules having increased expression in an intestinal polyp relative to a control. On this basis alone Applicants submit that the rejection of Claims 13 and 19 should be withdrawn.

The Combined References of Reinhard, Holmes, and Lee Do Not Provide a Suggestion or Motivation to Modify the References or Combine the Reference Teachings

While Applicants assert that the combined references of Reinhard, Holmes, and Lee do not teach every limitation of Claims 13 or 19, Applicants submit that even assuming *arguendo* that the combined references did teach every element, the combined references do not provide a suggestion or motivation to modify or combine the teachings of the references to obtain the invention as recited in Claims 13 or 19. Neither Reinhard nor Holmes teach or suggest that any additional genes other than the one gene disclosed in each respective reference should be evaluated in order to identify an intestinal polyp, and they do not suggest that at least three informative nucleic acid molecules selected from the nucleic acid molecules in Figures 1A-1U should be examined, as recited in Claims 13 and 19. Lee does not teach or suggest that the IGFBP-1 gene is expressed in intestinal tissue or that the IGFBP-1 gene has increased expression in intestinal polyps relative to normal tissue. In addition, Lee does not teach or suggest that the IGFBP-1 gene can be used to identify an intestinal polyp according to the methods of Claims 13 or 19. Thus, the combination of Reinhard, Holmes, and Lee provides no suggestion or motivation to combine or modify any of the references to obtain the invention as recited in Claims 13 or 19.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

1. (Amended) A method of identifying an intestinal polyp comprising the steps of:
   a) obtaining a nucleic acid sample derived from intestinal tissue; and
   b) determining [a gene] an expression profile from [a gene] expression [product] products of at least [one] three informative [gene] nucleic acid molecules having increased expression in an intestinal polyp relative to a control,

   wherein increased expression of said [gene] nucleic acid molecules in said sample is indicative of an intestinal polyp.

2. (Amended) [A] The method according to Claim 1, wherein the intestinal polyp is an upper intestinal polyp or a colonic polyp.

3. (Amended) [A] The method according to Claim 1, wherein the nucleic acid sample derived from intestinal tissue is derived from upper intestinal tissue or colonic tissue.

4. (Amended) [A] The method according to Claim 1, wherein the [gene] expression product is DNA.

5. (Amended) [A] The method according to Claim 1, wherein the [gene] expression product is mRNA.

6. (Amended) [A] The method according to Claim 4, wherein the [gene] expression profile is determined utilizing specific hybridization probes.

7. (Amended) [A] The method according to Claim 5, wherein the [gene] expression profile is determined utilizing specific hybridization probes.

8. (Amended) [A] The method according to Claim 6, wherein the [gene] expression profile is determined utilizing oligonucleotide microarrays.

9. (Amended) [A] The method according to Claim 7, wherein the [gene] expression profile is determined using oligonucleotide microarrays.

10. (Amended) [A] The method according to Claim 1, wherein the [gene] expression product is a polypeptide.

11. (Amended) [A] The method according to Claim 10, wherein the [gene] expression profile is determined utilizing antibodies.

12. (Amended) [A] The method according to Claim 1, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of apoptosis genes, cell cycle genes, tumor suppressor genes, cell adhesion genes, transcription related genes, and inflammation genes.

13. (Amended) [A] The method according to Claim 1, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of the [genes] nucleic acid molecules in Figures 1A-1U.

14. (Amended) A method of identifying an intestinal polyp comprising the steps of:

a) obtaining a polypeptide sample derived from intestinal tissue; and

b) determining [a gene] an expression profile from [a gene] expression [product] products of at least [one] three informative [gene] nucleic acid molecules having increased expression in an intestinal polyp relative to a control, said [gene] expression [product] products being [a polypeptide] polypeptides,

wherein increased expression of said [gene] expression [product] products in said sample is indicative of an intestinal polyp.

15. (Amended) [A] The method according to Claim 14, wherein the intestinal polyp is an upper intestinal polyp or a colonic polyp.

16. (Amended) [A] The method according to Claim 14, wherein the polypeptide sample derived from intestinal tissue is derived from upper intestinal tissue or colonic tissue.

17. (Amended) [A] The method according to Claim 14, wherein the [gene] expression profile is determined utilizing antibodies.

18. (Amended) [A] The method according to Claim 14, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of apoptosis genes, cell cycle genes, tumor suppressor genes, cell adhesion genes, transcription related genes, and inflammation genes.

19. (Amended) [A] The method according to Claim 14, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of the [genes] nucleic acid molecules in Figures 1A-1U.

20. (Amended) A method of identifying an intestinal polyp comprising the steps of:

a) obtaining a nucleic acid sample derived from intestinal tissue; and

b) determining [a gene] an expression profile from [a gene] an expression product of at least one informative [gene] nucleic acid molecule having decreased expression in an intestinal polyp relative to a control,

wherein decreased expression of said [gene] nucleic acid molecule in said sample is indicative of an intestinal polyp.

21. (Amended) [A] The method according to Claim 20, wherein the intestinal polyp is an upper intestinal polyp or a colonic polyp.

22. (Amended) [A] The method according to Claim 20, wherein the nucleic acid sample derived from intestinal tissue is derived from upper intestinal tissue or colonic tissue.

23. (Amended) [A] The method according to Claim 20, wherein the [gene] expression product is DNA.

24. (Amended) [A] The method according to Claim 20, wherein the [gene] expression product is mRNA.

25. (Amended) [A] The method according to Claim 23, wherein the [gene] expression profile is determined utilizing specific hybridization probes.

26. (Amended) [A] The method according to Claim 24, wherein the [gene] expression profile is determined utilizing specific hybridization probes.

27. (Amended) [A] The method according to Claim 25, wherein the [gene] expression profile is determined utilizing oligonucleotide microarrays.

28. (Amended) [A] The method according to Claim 26, wherein the [gene] expression profile is determined using oligonucleotide microarrays.

29. (Amended) [A] The method according to Claim 20, wherein the [gene] expression product is a polypeptide.

30. (Amended) [A] The method according to Claim 29, wherein the [gene] expression profile is determined utilizing antibodies.

31. (Amended) [A] The method according to Claim 20, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of apoptosis genes, cell cycle

genes, tumor suppressor genes, cell adhesion genes, transcription related genes, and inflammation genes.

32. (Amended) [A] The method according to Claim 20, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of the [genes] nucleic acid molecules in Figures 1A-1U.

33. (Amended) A method of identifying an intestinal polyp comprising the steps of:

a) obtaining a polypeptide sample derived from intestinal tissue; and

b) determining [a gene] an expression profile from [a gene] an expression product of at least one informative [gene] nucleic acid molecule having decreased expression in an intestinal polyp relative to a control, said [gene] expression product being a polypeptide,

wherein decreased expression of said [gene] expression product in said sample is indicative of an intestinal polyp.

34. (Amended) [A] The method according to Claim 33, wherein the intestinal polyp is an upper intestinal polyp or a colonic polyp.

35. (Amended) [A] The method according to Claim 33, wherein the polypeptide sample derived from intestinal tissue is derived from upper intestinal tissue or colonic tissue.

36. (Amended) [A] The method according to Claim 33, wherein the [gene] expression profile is determined utilizing antibodies.

37. (Amended) [A] The method according to Claim 33, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of apoptosis genes, cell cycle genes, tumor suppressor genes, cell adhesion genes, transcription related genes, and inflammation genes.

38. (Amended) [A] The method according to Claim 33, wherein one or more informative [genes] nucleic acid molecules is selected from the group consisting of the [genes] nucleic acid molecules in Figures 1A-1U.